

**What is claimed is:**

1. A method for identifying compounds that directly interact with a Smad protein or a Smad protein co-repressor to prevent protein-protein or protein-DNA interactions required  
5 for repression of transcription induced by TGF- $\beta$ , activin or bone morphogenetic protein signaling in cells comprising:

(a) determining a first level of transcription detected in cells in the presence of a Smad protein and a CtBP protein before addition of a test compound;

10 (b) contacting said cells with the test compound;  
and

(c) determining a second level of transcription detected in cells in the presence of a Smad protein and a CtBP protein after addition of the test compound, wherein a  
15 decrease in the level of repression of transcription induced by the presence of the Smad protein and the CtBP protein is indicative of the ability of the test compound to interfere with transcriptional repression and to prevent repression of transcription that is produced by a TGF- $\beta$ , activin, or bone  
20 morphogenetic protein signal in cells.

2. The method of claim 1 wherein transcription levels both before and after addition of the test compound are detected in cells in the presence of a Smad protein, a CtBP protein, and a co-repressor protein selected from the group  
25 consisting of Evi-1, TGIF, SIP1, and Schnurri.

3. The method of claim 1 wherein the Smad protein is *Drosophila* Mad or Medea.

4. The method of claim 1 wherein the CtBP protein is dCtBP, CtBP2 or any homologue of CtBP.

5. A composition identified by the method of claim 1.

6. A method for identifying a candidate gene that is  
5 directly and negatively regulated by TGF- $\beta$  signaling pathways through a CtBP protein comprising:

(a) determining a first level of TGF $\beta$ -regulated target gene expression in the presence of CtBP;

(b) determining a second level of TGF $\beta$ -regulated  
10 target gene expression in the absence of the CtBP protein; and

(c) comparing the first level of expression with the second level of expression, wherein dependence of TGF $\beta$ -regulated gene expression on the presence of the CtBP protein is indicative of the ability of the candidate gene to be  
15 directly and negatively regulated by CtBP working in conjunction with the Smad protein.

7. The method of claim 6 wherein the CtBP protein is dCtBP.

8. The method of claim 6 wherein the Smad protein is  
20 *Drosophila* Mad or Medea.